REMARKS

Applicants have amended Claims 5, 10, 13, 19, 45-47, 51, 56, 71-73, 76 and 81, and have canceled Claims 75, and 82-86 without prejudice. Enabling support for the amendments can be found in the application as filed, and therefore no new matter is contained in the amendments. Reconsideration of the present application and allowance of resulting Claims 4-20, 43-61, 70-74, and 76-81 is respectfully requested in view of the amendments and following remarks.

I. Claim Rejections under 35 U.S.C. § 112, first paragraph, enablement requirement

The Office Action has rejected Claims 4-20, and 43-61 under 35 U.S.C. §112, first paragraph as failing to comply with the enablement requirement. The Office Action states "while the specification discloses the use of human cord blood fractions that have been used directly upon thawing (cord blood mononuclear cells) or treated in cultures for a week with various trophic factors (BDNF, NGF, EGF + bFGF) prior to transplantation, the claims cover the preparation of a great variety of cell compositions, including terminally-differentiated cells, which the specification does not teach how to use. The human cord blood fractions used directly upon thawing are not the cells produced by the claimed methods, but rather appear to be the starting material for use in the claimed method. With regard to the cells that were cultured with various trophic factors, the specification does not disclose the phenotype of these cells and the claims require the production of "neural cells."" Applicants respectfully traverse the rejection as follows.

The specification teaches the use of the mononuclear fraction from cord blood and the use of neural cells derived therefrom for the treatment of neural damage. Page 58 of the instant specification discloses the administration of cord blood mononuclear cells or cells that had been treated with various trophic factors prior to transplantation into rats with a temporary stroke model.

In addition, the specification teaches the culture of human cord blood with a number of differentiation agents in order to produce neural cells, and compositions comprising the neural cells derived from human cord blood cells. For example, the instant specification teaches the isolation of human cord blood cells, which were thawed and plated in minimal essential medium (page 37). After 24-72 hours, the medium was replaced with serum free "Neural Proliferation Medium" consisting of N2 medium, supplemented with glucose, insulin, transferring, progesterone, putrescine, selenium chloride, glutamine, sodium bicarbonate, HEPES, herarin, EGF and bGHG. The cultures were then exposed to "Neural Differentiation Medium," which was the Neural Proliferation Medium without EGF and bFGF, but instead containing retinoic acid (RA) plus NGF. RNA was isolated from the cells treated with or without the RA+NGF, and the cells were also examined with antibodies to neural markers. Cells treated with RA+NGF showed higher levels of RNA and protein for a number of neural markers than was observed in control cells treated with DMEM. For example, using a gene chip, a total of 322 genes were up-regulated or down-regulated by at least a factor of 2 (pg. 40, lines 5-7). The greatest degrees of up-regulation were noted for pleiotrophin, glypican-4, neuronal pentraxin II, neuronal growth associated protein 43, and neuronal PAS1 (page 40, lines 6-15). By immunohistochemistry, it was shown that a significant proportion of cells in the RA+NGF treated cultures were positive for Musashi-1, β-tubulin III, GFAP, while the DMEM treated cells were not immunoreactive for these markers. Densitometric analysis of Western blots showed

that NGF+RA treatment increased protein expression of Musashi-1, β-tubulin III, pleiotrophin and NeuN (page 40, lines 10-25). This example demonstrates that neural cells are readily derived from human cord blood cells using differentiation agents. The cells express a number of neural markers, including nestin, a marker for neuronal precursors, GFAP, a marker for astrocytes, and NeuN, a neuron specific marker. As such, Applicants have demonstrated that culturing human cord blood cells with trophic factors results in the production of neural cells that can readily be used for transplantation and for other purposes.

The Office Action further states "No working examples [are provided] that demonstrate a therapeutic effect upon transplantation of the claimed composition." Applicant respectfully traverses this assertion. Page 58 of the instant specification discusses the results of transplantation of neural cells (HUCB cells treated with RA+NGF) into ischemic rats, and notes that the rats treated with neural cells demonstrated improved motor coordination in comparison to rats that were not treated with donor cells.

Additionally, as noted in our previous response, the specification provides specific guidance for treating pathological conditions, such as by providing suggested methods of administration (pages 58-72), protocols for the preparation of donor cells and the implantation of the cells, including providing an estimated cell number of implantation (page 58, lines 19-25 and page 60, lines 7-10), providing the results of behavioral tests from animals with a stroke model that had been treated with HUCB or HUCB derived neural cells (page 60-61, 63-66), providing the protocols and results in brain injured animals of parenteral administration of HUCBC (pages 66-72).

Applicants are not required to isolate and identify every neural cell that can be derived from HUCB cells. Applicants have developed methods for deriving neural cells from HUCB cells that are useful in transplantation, and are also useful for generating specific neural

lineages, for the generation of proteins produced at various stages of cell development, and for permitting recombinant production of polypeptides. The exact types of neural cells produced will vary, however, the use of a particular type of neural cell is not critical to the nature of the invention. The identification of neural cells is routine for one of ordinary skill in the art, and is set out in the instant specification at page 14, line 21 through page 15, line 10.

For at least the foregoing reasons, and considering the amendments to the claims, Applicants respectfully request reconsideration and removal of the rejection and allowance of Claims 4-20, and 43-61.

II. Claim Rejections under 35 U.S.C. § 112, second paragraph, definiteness requirement

The Office Action has rejected Claims 4-20, 43-61, and 72-86 under 35 U.S.C. §112, second paragraph, as failing to comply with the definiteness requirement.

The Office Action states "Claims 4-20, 43-61, and 72-86" are indefinite in their recitation of "neural cells" because, as evidenced by the claim language of newly added Claim 75, Applicants apparently consider hematopoietic stem cells to constitute "neural cells." This interpretation is not conventional in the art and the specification does not provide a clear definition for the term "neural cells." Applicants respectfully traverse this rejection as follows.

Claims 75, and 82-86 have been canceled and therefore the rejection is moot with respect to those claims. By cancellation of these claims, applicants do agree with the Examiner's assertion but only to advance the prosecution of the present application. Applicants reserve the right to prosecute the subject matter in these claims in one or more continuation or divisional applications.

The term "neural cell" is clearly defined in the instant specification at page 14, lines 21-23. The specification defines "neural cells" as "cells having at least an indication of

neuronal or glial phenotype, such as staining for one or more neuronal or glial markers or which will differentiate into cells exhibiting neuronal or glial markers." As such, the term "neural cell" is clearly defined and would be readily understood by one of skill in the art. In addition, Applicants have canceled Claim 75. Applicants assert that the rejections have therefore been overcome.

Claims 72-81 were rejected as indefinite in their recitation of "increase" and "decrease." Claim 75 has been canceled and therefore the rejection is moot with respect to this claim. Applicants have amended Claims 72 and 81 to provide a reference state for "increase" and "decrease" and submit that the amendments overcome the rejections.

Claim 76 was rejected because one or more words appear to be missing. Applicants have amended Claim 76 to recite "[t]he isolated neural cell of claim 72" and submit that the amendment overcomes the rejection.

For at least the reasons described above, Applicants assert that the amendments overcome the rejection, and respectfully request reconsideration and removal of the rejections and allowance of Claims 4-20, 43-61, 72-74 and 76-81.

III. Claim Rejections under 35 U.S.C. § 102

The Office Action rejected Claims 72-86 under 35 U.S.C. §102(a) as being anticipated by Kopen et al. (1999). The Office Action states "Kopen et al. (1999) disclose that marrow stromal cells (MSCs, also mesenchymal stem cells) injected into the lateral ventricle of neonatal mice differentiated into astrocytes and neurons. Since mesenchymal stem cells are also present in umbilical cord blood, the cells disclosed by Kopen et al. meet all the claim limitations." Applicants respectfully traverse the rejection as follows.

Claims 75, and 82-86 have been canceled and therefore the rejection is moot with respect to those claims. Kopen et al. describes the injection of mouse marrow stromal cells into a mouse, where integration and differentiation of the bone marrow stromal cells into neural cells are observed. Kopen et al. does not disclose or suggest cells having the expression pattern recited in Claims 72-74, and 76-81. For at least this reason, Applicants respectfully submit that the cited reference does not teach or suggest every element of the claimed invention.

The Office Action rejected Claims 72-74 and 76-86 under 35 U.S.C. §102(b) as being anticipated by Dunbar et al. (1994). The Office Action states "In view of the claim language set forth in newly added Claim 75 reciting "wherein said neural cell is not a hematopoietic stem cell," it is evident that Applicants consider hematopoietic stems cells to constitute "neural cells" within Applicants interpretation of this term. Dunbar et al. discloses that hematopoietic stem cells were known in the prior art." Applicants respectfully traverse the rejection.

Claims 75, and 82-86 have been canceled and therefore the rejection is moot with respect to those claims. By cancellation of these claims, applicants do agree with the Examiner's assertion but only to advance the prosecution of the present application. Applicants reserve the right to prosecute the subject matter in these claims in one or more continuation or divisional applications. Dunbar et al. does not teach or suggest a neural cell having the expression pattern recited in any of Claims 72-74 and 76-81. For at least these reasons, Applicants submit that the amendments overcome the rejections and respectfully request reconsideration and allowance of the amended claims.

The Office Action rejects Claims 82-86 under 35 U.S.C. §102(b) as being anticipated by Reynolds et al. (1992). The Office Action states "Reynolds et al. (1992) disclose neurons, astrocytes, and neuroepithelial stem cells. All three cell types qualify as "neural cells" as instantly claimed." Claims 82-86 have been canceled and therefore the rejection is moot with respect to those claims.

The Office Action rejected Claims 72-86 under 35 U.S.C. §102(b) as being anticipated by Azizi et al. (1998). The Office Action states "Azizi et al. (1998) disclose human marrow stromal cells (MSCs). They also examined the effects of direct injection of human MSCs into the brains of rats and found that the cells migrated from the injection site along known pathways for migration of neural stem cells to successive layers of the brain. Since mesenchymal stem cells are also present in umbilical cord blood the cells disclosed by Azizi et al. meet all the claim limitations."

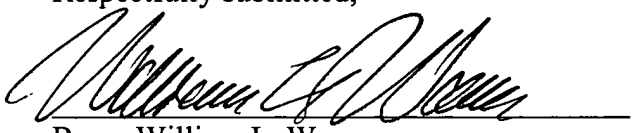
Claims 75, and 82-86 have been canceled and therefore the rejection is moot with respect to those claims. Azizi et al. describes the injection of human marrow stromal cells into a rat, where integration and differentiation of the bone marrow stromal cells into neural cells are observed. Azizi et al. does not disclose or suggest cells having the expression pattern recited in Claims 72-74, and 76-81. Additionally, Azizi et al. does not disclose neural cells that are obtained from umbilical cord blood. For at least these reasons, Applicants respectfully submit that the cited reference does not teach or suggest every element of the claimed invention.

For at least these reasons, Applicants submit that the amendments overcome the §102 rejections and respectfully request reconsideration and allowance of the amended claims.

For at least the foregoing reasons, Applicants respectfully request reconsideration and removal of the rejections and allowance of Claims 4-20, 43-61, 70-74, and 76-81. The foregoing is submitted as a full and complete Response to the Final Office Action mailed January 2, 2004. No additional fees are believed due; however, the Commissioner is hereby authorized to charge any additional fees that may be required, or credit any overpayment to Deposit Account No. 19-5029.

This Response places all claims in the present application in condition for allowance, and such action is courteously solicited. The Examiner is invited and encouraged to contact the undersigned attorney of record if such contact will facilitate an efficient examination and allowance of the application.

Respectfully submitted,



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